PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IB2005/000452	21.02.2005	09.03.2004

International Patent Classification (IPC) or both national classification and IPC
C07D223/22, C07D223/28

Applicant
CLARIANT INTERNATIONAL LTD

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/IB2005/000452

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-7
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-7
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-7
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following document:

D1: DE 20 11 087 A1 (CIBA-GEIGY AG, BASEL) 24 September 1970 (1970-09-24)

D2: DATABASE CAPLUS [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; HAASZ, FERENC ET AL: "Improved process for producing 5-carbamoyl-10-oxo-10,11-dihydro-5H- dibenz[b,f]azepine" XP002306691 retrieved from STN Database accession no. 1994:164010

D3: HEINER ECKERT ET AL: "Triphosgene, a Crystalline Phosgene Sustitute" ANGEWANDTE CHEMIE. INTERNATIONAL EDITION, VERLAG CHEMIE. WEINHEIM, DE, vol. 26, no. 9, 1987, pages 894-895, XP002083416 ISSN: 0570-0833

V.1. Novelty:

The process for the preparation of Oxcarbazepine using triphosgene for the chlorocarbonylation reaction of 10-methoxy-5H-dibenzo[b,f]azepine has not been disclosed in the prior art.

Consequently, the subject-matter of claims 1-7 is novel (Article 33(2) PCT).

V.2. Inventive Step:

The documents D1 and D2 are regarded as being the closest prior art to the subject-matter of claim 1, and disclose a process for the preparation of Oxcarbazepine from 10-methoxy-5H-dibenz[b,f]azepine comprising the consecutive steps of chlorocarbonylation, ammonolysis, and hydrolysis. In the case of D1 the chlorocarbonylation is carried with phosgene as reagent and in D2 with diphosgene.

The subject-matter of claim 1 differs from these known processes in that triphosgene is used as chlorocarbonylation reagent.

The problem to be solved by the present application may therefore be regarded as the provision of a further process for the preparation of Oxcarbazepine.

Document D3 relates to triphosgene as being a crystalline, stable solid, easy to transport and store and as such, an excellent substitute for the highly toxic and gaseous phosgene.

In view of the teaching of D3 and D4, the skilled person would regard it a normal procedure to substitute phosgene or diphosgene in the known processes of D1 and D2 by the less toxic triphosgene.

However, the overall-yields achieved in D1 and D2 are 45% and 43,3%, respectively. The process of the present application using triphosgene reaches an overall-yield of 70%. This considerable improvement can be recognised as unexpected effect and hence the subject-matter of claims 1-7 is considered as involving an inventive step (Article 33(2) PCT).

V.3. Industrial Applicability:

The present application relates to the preparation of Oxcarbazepine which is useful as anticonvulsant. The subject matter of claims 1-7 is therefore considered as industrially applicable (Article 33(4) PCT).